**Amendments to the Specification:**

Please amend the specification as follows:

After the Application Title, please insert:

This application is a continuation-of PCT Application No. PCT/EP00/00690, filed January 28, 2000, which claims the benefit of EP99/101590.0, filed January 29, 1999.

Please replace paragraph starting at page 6, line 13, with the following rewritten paragraph:

The resulting peptide masses are searched by search programs (e. g. ~~http://~~prospector.ucsf.edu/ucsfhtml3.2/msfit.htm; ~~http://~~www.expasy.ch/tools/peptident.html) in sequence databases (EMBL, PIR, NCBI, MIPS, Swiss-Prot, OWL). By use of such mass fingerprints amino acid sequences can be deduced and sequenced. From these sequenced amino acid fragments degenerative oligonucleotides may be deduced and synthesized that may be used to screen, for example, genomic or cDNA libraries to identify and clone the corresponding GENE/cDNA.

Please replace paragraph starting at page 8, line 11, with the following rewritten paragraph:

In an even more preferred embodiment of the composition of the present invention said differentially expressed protein is 2-isopropyl malate synthase (Rv3710), s-adenosylmethionine synthase (metK, RV1392), succinyl-CoA synthase a-chain (sucD, RV0952), oxidoreductase of aldo/keto reductase family (Rv2971), oxidoreductase (Rv0068), elongation factor G (FusA2, Rv0120c), uridylate kinase (PyrH, Rv2883c), ABC-type transporter (RV1463), short chain dehydrogenase/reductase family (RV1856C), hydrolase (LinB, Rv2579), phosphoribosylamino-imidazole carboxylase catalytic subunit (PurE,

Rv3275c), hypothetical protein (Rv2557), hypothetical protein (Rv3407), hypothetical protein (Rv3881c), hypothetical protein (Rv2449c), hypothetical protein (Rv0036c), hypothetical protein (Rv2005c) or transcriptional regulator (Crp/Fr family) (Rv 3676). As shown in the appended examples, whereas 2-isopropyl malate synthase (Rv3710) is expressed in M. tuberculosis H37Rv, it is not detected and identified in M. bovis BCG. Furthermore, s-adenosylmethionine synthase (metK, RV1392), succinyl-CoA synthase a-chain (SUCD, Rv0952), oxidoreductase of aldo/keto reductase family (Rv2971) or oxidoreductase (Rv0068), represent protein species which are differentially expressed in M. tuberculosis H37Rv and M. bovis BCG and represent mobility variants. As intensity variants may be considered proteins corresponding to the Rv numbers Rv0652, Rv2429, Rv2428, RV0569, Rv0475, Rv3463, Rv3054c. As +/--variants may be considered Rv2883c, Rv0120c, Rv1463, Rv2579, Rv3275c, Rv3407, Rv3881c, Rv2449c, Rv0036c, Rv2005c or Rv3676. As shown in the appended examples, whereas elongation factor G (Rv0120c), uridylate kinase (Rv2883c), ABC-type transporter (Rv1463), short chain dehydrogenase/reductase family protein (Rv1856c), 1,3,4,6-tetracholoro- 1,4,-cyclohexadiene hydrolase (Rv2579), phosphoribosylaminoimidazole carboxylase catalytic subunit (Rv3275c), hypothetical protein (Rv2557), and hypothetical protein (Rv3407) are expressed in M. tuberculosis H37Rv and M. tuberculosis Erdman, they are not detected in M. bovis BCG Chicago and M. bovis BCG Copenhagen. Furthermore, protein spot A607 in M. tuberculosis H37Rv and the corresponding spot A148 in M. tuberculosis Erdman have no counterparts in M. bovis BCG Chicago and M. bovis BCG Copenhagen. This protein was identified herein as the hypothetical protein Rv3881c. Furthermore, spots C434 from M. tuberculosis H37Rv and the corresponding spot C508 from M. tuberculosis Erdman have no counterparts in M. bovis BCG Chicago and M. bovis Copenhagen. They were identified as a hypothetical protein (Rv2005c). Rv2005c occurs at the 2-DE pattern in another form at a different position in all four strains. Additionally, the spots B69, C176, D12 and D115 of M. tuberculosis H37Rv with their counterparts in M. tuberculosis Erdman, B54, C404, D115 and D130, respectively, have no counterparts in M. bovis BCG Chicago and M. bovis BCG Copenhagen. B69 was identified as a hypothetical protein (Rv2449c). C176 was identified as a hypothetical protein (Rv0036c). D12 and D115 of M. tuberculosis H37Rv were identified as transcriptional

regulator (Crp/Fnr family) (Rv3676). As will be described herein below these proteins/protein species might serve, inter alia, in pharmaceutical and diagnostic compositions. Cole (Nature 393 (1998), 537) published the complete sequence of the M. tuberculosis H37Rv genome and identified a total of 3924 individual genes which were classified according to the classification of Riley (Microbiol. Rev. 57 (1993), 862). Identifications of this putative genes were performed by homology searches of deduced open reading frames from other microorganisms. Therefore, the term "Rv numbers" as employed herein corresponds to clearly defined nucleic acid sequences (deduced open reading frames) as describes in Cole et al., (loc. cit.). However, for most of the identified putative genes of M. tuberculosis, it is not clearly shown that they are actually expressed. additional sequence information on mycobacterial genes is also available from the Sanger Centre, U. K. Under ~~http://~~www.sanger.ac.uk/Projects/M_tuberculosis/ information on the genomic sequence of M. tuberculosis is available. Therefore, the "Rv-numbers" not only refer to nucleic acid sequences but also to protein sequences as deposited in the Sanger database. Further information on M. tuberculosis sequence is available from the Institut Pasteur, Paris under ~~http://~~bioweb.pasteur.fr/GenoList/TubercuList/.

Please replace paragraph starting at page 10, line 7, with the following rewritten paragraph:

The term "antigenic fragment", as used herein, refers to the ability of said fragment to elicit an immune response (e. g. humoral or cellular) in a subject, such as a human, and/or in a biological sample. These fragments may consist entirely of the antigenic and/or immunogenic portion of the protein or may contain additional sequences. The additional sequences may be derived from said protein or may be heterologous, and such additional sequences may (but need not) be antigenic and/or immunogenic. The antigenicity of an amino acid sequence can be deduced/predicted by methods known to the person skilled in the art as for example described in Parker, J. Immunol. 152 (1994), 163 (~~http://~~bimas.dcrt.nih.gov:80/molbio/hla_bind/), Meister, Vaccine 13 (1995), 581-591 or Bull,

Biochem. Biophys. 161 (1974), 665- 670. Furthermore, computer predictions may be employed to elucidate hydrophilicity and/or antigenicity of amino acid sequences and stretches. Such computer programs may be Garnier analysis of the on the plot v. 2.5e package, the GCG-software derived from HGMP resource Center Cambridge (Rice (1995) Programme Manual for the EGCG package, Cambridge (B10 IKQ, England) or the programme based on Kyte/Dolittle, J. Mol. Biol. 157 (1982), 105-132 (see also ~~http://~~www.expasy.ch/cgi-bin/protscale.pl).

Please replace paragraph starting at page 16, line 7, with the following rewritten paragraph:

Most preferably said nucleic acid molecule is the nucleic acid molecule as disclosed under said Rv-number under ~~http://~~www.sanger.ac.uk/Projects/M_tuberculosis or ~~http://~~bioweb.pasteur.fr/GenoList/TubercuList. However, the present invention relates also to compositions comprising at least one Nucliec acid molecule which hybridizes under stringent conditions to the complementary strand of the nucleic acid molecule of any of the above cited Rv-numbers. "Stringent conditions" are preferably conditions as described in Sambrook (Molecular Cloning, A Laboratory Manual, 2nd edition (1989), Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY).

Please replace paragraph starting at page 30, line 30, with the following rewritten paragraph:

Identification of proteins separated by 2-DE has been reviewed (Patterson (1995), Electrophoresis 16: 1791; P. Jungblut (1996), Electrophoresis 17: 839; Jungblut (1997), Mass Spectrometry Reviews 16: 145) 2-DE combines isoelectric focusing in the first dimension with SDS-PAGE (Sodiumdodecyl sulfate polyacrylamide gel electrophoresis) in the second dimension. The proteins are separated by two independent parameters, charge and molecular mass. Single amino acid changes may be detected. The resolution power of the used

technique (gel size 23 cm x 30 cm) is about 5000 protein species, which should be sufficient for a microorganism with about 3700 genes like Mycobacterium tuberculosis or bovis. The term protein species is defined as the smallest unit of a protein classification, defined by its chemical structure. In-gel tryptic digestion (Otto (1996), Electrophoresis 17: 1643) and MALDI-MS peptide mass fingerprinting (Henzel (1993), Proc. Natl. Acad. Sci. U. S. A. 90: 5011; Pappin (1993), Current Biology 3: 327; Mann (1993), Biol. Mass Spectrom. 22: 338; James (1993), Biochem. Biophys. Res. Commun. 195: 58) with the possibility of sequencing by post-source decay MALDI-MS (Spengler (1992), Rapid Commun. Mass Spectrom. 6: 105) were chosen in order to identify the first 263 proteins, with a priority for high intensity proteins and for variants between the investigated mycobacteriai strains. Peptide mass fingerprints were searched using the program MS-FIT (~~http://~~prospector.ucsf.edu/ucsfhtml/msfit.htm) reducing the proteins of the NCBI database to the mycobacteriai proteins and to a molecular mass range estimated from 2-DE +/-20%, allowing a mass accuracy of 0.1 Da for the peptide mass. In the absence of matches the MOLECULAR mass window was extended. Partial enzymatic cleavages leaving two cleavage sites, oxidation of methionine, pyro-glutamic acid formation at N-terminal giutamine and modification of cysteine by acrylamide were considered in these searches.

Please replace paragraph starting at page 32, line 2, with the following rewritten paragraph:

Data obtained as described in Example 2 and 8 are shown in Figures 1 to 5 and illustrated in Tables 1 to 4. Further information is available via internet (~~http://~~www.mpiib-berlin.mpg.de/2DPAGE/). The 2D-PAGE database complies with all rules according to the World 2D-PAGE guidelines for building a federated database (Appel (1996), Electrophoresis 17: 540). To navigate through the database, a Java compatible browser is required (e. g. Netscape 4.0 or internet Explorer 4.0). The program consists of common gateway interface (CGI) scripts written in PERL. One set of data comprises three files. The link between the image file, the map file and the rational data file is built by their names. The image file is a

high density scan of the 2-D gel. The map file describes the location and the size of the spots as polygons. The rational data file is a document in Microsoft Access format that is connected to the WWW server by an Open Database Connectivity (ODBC) driver from MySQL. This connection ensures that after a single transfer of all data, no further maintenance and administration work is required. The rational data file is located on a micro-computer with IP address at any location of choice. The Hyper Text Markup Language (HTML) documents displayed via internet are dynamically generated on the basis of the available data for each individual session. Properties of proteins are presented in annotation spot windows. An example for such an annotation is: Spot ID: C191, Mr (2-DE): 27100, Mr (theoretical) 28160, pi (2-DE) 4.7, Identification Method PMF/PSD, Sequence coverage 35 %, Protein name electron transfer flavoprotein beta subunit, short name fixA, Rv-No Rv3029c, EMBL: Z99263, NCBI: 2414529, Ident. No MLCB637, Gene No MLCB637.03. The EMBL and NCBI Nos have hyperlinks to obtain easily more information.

Please replace paragraph starting at page 41, line 26, with the following rewritten paragraph:

As described herein above (see Example 5) two proteins could be identified which are expressed in M. tuberculosis H37Rv, but not in M. bovis BCG: L-alanine- dehydrogenase (40 kDa antigen; Rv 2780) and MPT64 (Rv 1980c). The absence of alanine dehydrogenase in BCG has been described earlier (Andersen et al. Infect.Immun. 60,2317 (1992)) and was confirmed by this approach. MPT64 (Rv1980c) is a CSN protein and is a known inducer of delayed type hypersensitivity responses in guinea pigs (S. H. K. Kaufmann and P. Andersen, in "Chemical Immunology: Immunology of Intracellular Parasitism" (Ed. F. Y. Liew), 1998: 21-59.). This protein was absent in the 2-DE patterns of BCG. This example illustrates the potential of the here described method for proteome analysis on strains of pathogenic organisms.

Please replace paragraph starting at page 42, line 11, with the following rewritten paragraph:

The 2-DE patterns of all four strains investigated (H37Rv, Erdman, Chicago and Copenhagen) are very conservative. The evaluation of 2-DE patterns comparing four strains of microorganism is difficult and time-consuming. In a second approach, therefore, the further analysis concentrated on +/-differences between the virulent strains as compared with the non-virulent strains. This investigation confirmed the results described in the examples described herein above. However, additional proteins Rv1511 (RD6), Rv1980c (RD2), Rv0222 (RD4), Rv1512 (RD6), Rv1978 (RD2), Rv2658c (RD13), Rv3875 (RD1), and Rv2074 (RD12) were found to be differentially expressed, confirming results from a comparison of the genome of M. tuberculosis with M. bovis by DNA Microarray (Science 284 (1999), 1520), where the loss of 16 regions (RD) in M. bovis BCG as compared to M. tuberculosis was described. Additionally, proteins occurring only in M. tuberculosis H37Rv and M. tuberculosis Erdman, but absent in Mycobacterium bovis BCG Chicago and Mycobacterium bovis BCG Copenhagen could be defined. These proteins COULD not be predicted by genomic investigations and comprised elongation factor G (Rv0120c), uridylate kinase (Rv2883c), ABC-type transporter (Rv1463), short chain dehydrogenase/reductase family protein (Rv1856c), 1,3,4,6-tetrachloro-1,4,- cyclohexadiene hydrolase (Rv2579), phosphoribosylaminoimidazole carboxylase catalytic subunit (Rv3275c), hypothetical protein (Rv2557), and hypothetical protein (Rv3407). The sectors where these proteins occur in the virulent strains are shown in Figure 5. The assignment of these protein species to their spot numbers and the link to the NCBI sequence database (~~http://~~www.ncbi.nlm.nih.gov/) by their accession No. are shown in Table 4.